

**REMARKS**

Claims 1, 2, 7-9 and 24-25 are pending in the application. Each of the claims has been rejected.

Upon entry of the Amendment, claims 2, 9 and 24-25 will be canceled, claims 26-28 added, and claims 1, 7, 8 and 26-28 will be pending.

The subject matter of claim 2 is being incorporated into claim 1.

Support for new claims 26-28 may be found in claims 1, 7 and 8, and in Example 7 (page 19) of the specification. The correspondence between the “caudate-putamen”, “CPU” and “corpus striatum” is provided in the initial Remarks to the Amendment filed August 13, 2010 in the application.

No new matter has been added. Entry of the amendment is respectfully requested.

**I. Rejection Under 35 U.S.C. §103**

At page 2 of the office action, the rejection of claims 1, 2, 7-9, 24 and 25 as being unpatentable under 35 U.S.C. §103(a) over Elgersma (2002), Wang (2003), Hanson (1994) and Sutoo (2002) has been maintained.

As a basis for the rejection, the Examiner stated in the office action dated July 9, 2009, that the “claimed knock-in animals are essentially disclosed by Wang et al with the exception of the phenotype limitation in claim 2” (page 5, office action dated July 9, 2009), that the use of the mutant of Hanson with the knock-in animals of Wang or Elgersma would have been obvious, and that the skilled artisan would have been motivated to produce the claimed knock-in animals to further knowledge on the role of CaMKII $\alpha$  in memory and learning. The Examiner concludes that “the totality of the prior art teaches the predictable generation of CaMKII $\alpha$  mutants with the claimed activity.”

Applicants respectfully traverse the Examiner’s position for the reasons of record set forth in the Amendment filed November 9, 2009, and for the following additional reasons.

In particular, Applicants note that courts in the U.S. have repeatedly found the presence of an unexpected property to be evidence of non-obviousness. The reverse is also true as the absence of an expected property can be evidence of non-obviousness. The amount of evidence needed to establish unexpected results needs to be sufficient to establish “that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance.” *Ex parte Gelles*, 22 USPQ2d 1318, 1319 (BPAI, 1992).

Applicants respectfully assert that the recited characteristics of the knockin animals of the pending claims are unexpected and unpredictable in view of the cited art. In particular, evidence that neuronal activity (claim 1) and cytochrome oxidase activity (claim 26) are lower in the nucleus accumbens, while unchanged in both the cerebral cortex and caudate-putamen, in comparison to wild-type animals, is both an unexpected and unpredictable property.

As described in the specification of the instant application, the inventors established the surprising finding that the claimed knockin mice exhibit lower neuronal activity in the nucleus accumbens in comparison to that of wild-type mice, while there is no substantial difference in neuronal activities in the cerebral cortex and caudate-putamen in comparison to wild-type counterparts. The combination of art cited by the Examiner neither teaches nor suggests such characteristics for the knockin mouse of the present invention. The corresponding findings with respect to the levels of cytochrome oxidase activity (recited in new claim 26) are equally surprising. The skilled artisan would have been unable to predict that differential levels of neuronal activity in different parts of the brain would result from a single amino acid change in CaMKII $\alpha$ . Similarly, a skilled artisan would have been unable to predict differential levels of cytochrome oxidase activity in different parts of the brain would result from the same mutation.

Given this evidence of non-obviousness, reconsideration and withdrawal of the rejection is earnestly solicited.

## II. Conclusion

In view of the above amendments and remarks, Applicants respectfully request a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Roylance, Abrams, Berdo & Goodman LLP  
1300 19th Street NW, Suite 600  
Washington, DC 20036-1649  
Voice: 202-530-7373  
Fax: 202-659-9344

Respectfully submitted,

/Drew Hissong/

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Drew Hissong  
Registration No. 44,765

Date: August 24, 2011

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Patent & Trademark Office

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